Remarks

Claims 1, 6-8, 15, 21 and 33 are pending in the instant application. Claims 1 and 15 have been amended in view of the Examiner's rejections. Applicants assert that these amendments raise no issues of new matter. Basis for these amendments can be found at least on page 10 line 15, and page 11, line 5 of the specification. Claims 6 has been amended to comply with the Examiner's objection to form regarding the lack of a period at the end of Claim 6. Claim 7 has been withdrawn and amended per 37 CFR 1.121(e)(2) to comply with the Examiner's objection to form regarding the lack of a period at the end of Claim 7. Claim 21 has been withdrawn. Applicants respectfully request entry of the amendments and allowance of the claims in view of these amendments and the remarks below.

Election/Restrictions

Applicants acknowledge the withdrawal of the restriction requirement and entry of the proposed amendment to the claims made August 20, 2007. Applicants assert that in view of the further amendments to the claims and remarks below, the species for EXAMPLE 30, and Claims 1, 6, 8, 15 and 33 are appropriately allowed, and thus respectfully request rejoinder of Claims 7 and 21.

Claim Rejections: 35 USC 103(a)

The Examiner has rejected Claims 1, 6, 8, 15 and 33 as obvious under 35 USC 103(a) in view of Cheshire *et al.* Applicants respectfully submit that neither the instant claims nor the elected species of EXAMPLE 30 are obvious in view of this reference.

<u>Graham v. John Decre Co.</u>, 383 U.S. 1, 148 USPQ 459 (1966) describes the factual inquiries that are applicable in determining obviousness:

- 1. Determining the scope and contents of the prior art.
- 2. Ascertaining the differences between the prior art and the claims at issue.
- 3. Resolving the level of ordinary skill in the pertinent art.
- Considering objective evidence present in the application indicating obviousness or nonobviousness

Applicants discuss each factor below as it relates to the instant application and the above stated reference

1. Determining the scope and contents of the prior art.

On Page 11 of Official Action dated September 5, 2007, the Examiner states that Cheshire et al. teaches Compound A as seen in Figure A below:

Figure A.

2. Ascertainment of the difference between the prior art and the claims

The Examiner has asserted that the difference between the prior art of Cheshire et al. and the instantly claimed compounds is that the compound of Cheshire et al. is a position isomer of the compound depicted in EXAMPLE 30 of the instant application. Moreover, the Examiner cites Ex parte Henkel, 130 USPQ 474 and Ex parte Weston, 121 USPQ 429, for the notion that position isomers are generally of sufficiently close structural similarity that there is a presumed expectation that such compound will possess similar properties. However, applicants, respectfully disagree. Chesire et al. describes the compound 3-(2,5-dichlorophenoxy)-N-methyl-1-hexamine, and other compounds, all which require a 2,5-substituted phenyl moiety, whereas EXAMPLE 30 describes a 2,4-substituted phenoxypropylamine. In addition, the instant claims as currently amended are drawn to phenoxyproplyamines which may have a variety of substitution patterns, as seen in Figure B below.

Figure B.

3. Lack of rationale and motivation for a Finding of Prima Facie Obviousness

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP §2143. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Further, "in addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of 'adequate support in the prior art' for the change in structure." Takeda Chem. Indus. v. Alphapharm Pty., Ltd., 83 USPQ2d 1169 at 1174 (Fed. Cir. 2007) (citing In re Grabiak, 769 F.2d 729, 731-32 (Fed. Cir. 1985) (emphasis added). As such, "in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." Id at 1174 (emphasis added). The United States Court of Appeals for the Federal Circuit has recently clarified that "in order to find a prima facie case of unpatentability in such instances, a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention' [is] also required." Id. at 1174 (internal citations omitted, emphasis added).

a. No teaching, or suggestion to make the species elected in view of Cheshire et al.

Applicants assert that there is no teaching or knowledge in the art to modify the required 2,5-substitution pattern of the phenoxypropylamines of Cheshire et al. to arrive at the 2,4-substituted compound of EXAMPLE 30. Any teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Nothing in the disclosure of Cheshire et al. indicates that Compound A above is the most desirable starting point for modification to develop further compounds that have similar properties. Takeda, 83 USPQ2d at 1156. Furthermore, the Examiner has not pointed to any art which indicates the desirability of "ring-walking" a substituent from the 5 position as described in Cheshire et al. to the 4 position of the compound of EXAMPLE 30. Takeda, 83 USPQ2d 1179.

Lastly no art as been cited as demonstrating the interchangeability of 2,5-substituted phenoxypropylamines with 2,4-substituted phenoxypropylamines. Thus there is no motivation to alter the substitution pattern on the phenyl ring on the left side of the compounds disclosed in Cheshire et al. to arrive at the compound of EXAMPLE 30.

b. No teaching, or suggestion to make the claimed compounds in view of Cheshire et al.

Applicants assert that there is no teaching or knowledge in the art to modify the required 2,5-substitution pattern of the phenoxypropylamines of Cheshire et al. to arrive at the 2,4substituted phenoxyproplyamines, 2,3,4- phenoxypropylamines and 2,4,6-phenoxypropylamines instantly claimed. Any teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Nothing in the disclosure of Cheshire et al. indicates that Compound A above is the most desirable starting point for modification to develop further compounds that have similar properties. Takeda, 83 USPQ2d at 1156. In addition, compounds of Cheshire et al. require substitution in the 2 and 5 positions, whereas the instantly claimed compounds never allow substitution in both of these positions simultaneously. The Examiner has pointed to no art demonstrating the motivation to modify 2.5substituted compounds described in Cheshire to arrive at any of the substitution patterns of the present invention. Lastly no art as been cited as demonstrating the interchangeability of 2.5substituted phenoxypropylamines with 2,3,4-, 2,4,6-, or 3,4,5-substituted phenoxypropylamines. Thus there is no motivation to alter the substitution pattern on the phenyl ring on the left side of the compounds disclosed in Cheshire et al. to arrive at the compounds of the present invention.

In view of the above arguments, Applicants assert that the instantly claimed compounds are not obvious in view Cheshire *et al.* under 35 U.S.C §103(a). Applicants respectfully request allowance of Claims 1, 6, 8, 15, and 33.

Claim Objections

The Examiner also objected to Claims 1, 6, 8, 15, and 33 for containing non-elected subject matter. Applicants assert the compound of EXAMPLE 30 was elected for the "sole purpose of examination." See page 6 of the August 20, 2007 REPLY UNDER 37 C.F.R. 1.111 & AMENDMENT UNDER 37 C.F.R. 1.121 to the Office Action dated July 20, 2007. In view of the arguments above, applicants respectfully submit that the elected species is allowable and request a

Serial No. 10/597-835

full examination of Claims 1, 6, 8, 15 and 33. See MPEP § 803.02.

Priority

Applicants respectfully request acknowledgment of priority. This is the national phase application, under 35 USC 371, for PCT/US2005/005226, filed 18 February 2005, which claims the benefit, under 35 USC 119(e), of US provisional application 60/550,259, filed 5 March 2004. Applicants assert that they have complied with the provisions of 35 USC 371 and 35 USC 119, See File History, and are thus entitled to claim the benefit of priority of the above-referenced applications.

Applicants respectfully request entry of the amendments to the claims described above and that the Examiner find the species of EXAMPLE 30 allowable. Moreover, applicants respectfully request that the examination of the claims, as amended, in their entirety. Applicants additionally request acknowledgement of their claim to priority. Finally, because Claims 1, 6, 8, 15 and 33 as amended are allowable, applicants request rejoinder of Claims 7 and 21. The Examiner is invited to contact the undersigned attorney should any questions arise as a result of the submission provided herein, or in the event any question arise at any point during examination.

Respectfully submitted,

/Tonya Combs/

Tonya Combs Attorney for Applicants Registration No. 57,909 Phone: 317-651-1266

Eli Lilly and Company Patent Division P.O. Box 6288 Indianapolis, Indiana 46206-6288

December 20, 2007